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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,810	07/10/2001	Kevin R. Mc Intosh	19226US01	7470

23446 7590 02/21/2008

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ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
02/21/2008	PAPER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte KEVIN R. MC INTOSH, JOSEPH D. MOSCA and ELENA N. KLYUSHNENKOVA

Appeal 2007-4243
Application 09/807,810
Technology Center 1600

Decided: February 21, 2008

Before DONALD E. ADAMS, RICHARD M. LEBOVITZ, and FRANCISCO C. PRATS, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of reducing a transplant recipient's immune response to donor tissue. The Examiner has rejected the claims as anticipated and obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm the anticipation rejection and reverse the obviousness rejection.

STATEMENT OF THE CASE

"Unfortunately, the immune system does not distinguish beneficial intruders, such as transplanted tissue, from those that are harmful, and thus

the immune system rejects transplanted tissue or organs" (Spec. 1). The Specification discloses, however, "that human fibroblasts can be used in transplantation to ameliorate a response by the immune system such that an immune response to an antigen(s) will be reduced or eliminated" (*id.* at 2).

Claim 1 is representative of the appealed claims and reads as follows:

> 1. A method of inducing a reduced immune response to donor tissue in a transplant recipient, comprising treating the recipient with at least one member selected from the group consisting of isolated fibroblasts and a supernatant from an isolated fibroblast culture in an amount effective to reduce an immune response in the recipient to the transplanted donor tissue.

Claims 1-33 are pending (*see* Br. 2).[1] Claims 3, 14, 15, 18, 23, 25, 29, and 33 have been withdrawn from consideration by the Examiner (*id.*). Claims 1, 2, 4-13, 16, 17, 19-22, 24, 26-28, and 30-32 are on appeal (*id.*).

The Examiner applies the following documents in rejecting the claims:

Bruder US 5,736,396 Apr. 7, 1998

R. J. Soiffer et al., *CD6-Depleted Allogeneic Bone Marrow Transplantation for Acute Leukemia in First Complete Remission*, 89 Blood 3039-3047 (April 15 1997).

J. J. Donnelly et al., *A Soluble Product of Human Corneal Fibroblasts Inhibits Lymphocyte Activation. Enhancement by Interferon-gamma*, 56 Exp. Eye Res. 157-165 (1993).

[1] Appeal Brief filed February 2, 2006.

The following rejections are before us for review:

Claims 1, 2, 4, 5, 8, 9, 11-13, 16, 17, 19, 21, 24, 26-28, 30, and 32 stand rejected under 35 U.S.C. § 102(b) as anticipated by Soiffer, as evidenced by Bruder (Ans. 3-4).

Claims 6, 7, 10, 20, 22, and 31 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Soiffer and Donnelly (Ans. 4-6).

ANTICIPATION

ISSUE

The Examiner states that Soiffer describes "a method of inducing a reduced immune response to donor tissue in a bone marrow transplant (BMT) recipient . . ., comprising treating (or contacting) the recipient with allogeneic (donor derived) fibroblasts" (Ans. 4). Citing Bruder to "establish[] that bone marrow includes fibroblasts," the Examiner reasons that "any BMT recipient would also receive donor derived fibroblasts" (*id.*).

The Examiner contends that the fibroblasts present in Soiffer's transplanted bone marrow are "isolated" as required by claim 1 because "'isolated' can 'be defined as separated or detached, thus, the fibroblasts need not be purified but only separated from their original source, i.e., the donor's bone'" (Ans. 8 (quoting Final Rejection 3)).

Appellants contend that Soiffer does not anticipate claim 1 because the fibroblasts present in Soiffer's transplanted bone marrow are not "isolated" (Br. 4-6). Rather, Appellants argue, "when read in the context of the specification, the term 'isolated' does not read upon the mere separation of the fibroblasts from bone, as the Examiner asserts" (*id.* at 6).

The issue with respect to this rejection, therefore, is whether the Examiner erred in finding that claim 1's recitation of "treating the

[transplant] recipient with . . . isolated fibroblasts" encompasses Soiffer's process of treating patients with bone marrow that contains fibroblasts.

PRINCIPLES OF LAW

It is well settled that "[t]o anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997). It is also well settled that during examination, the PTO must interpret terms in a claim using "the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification." *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997).

However, "while 'the specification [should be used] to interpret the meaning of a claim,' courts must not 'import[ ] limitations from the specification into the claim.' . . . [I]t is improper to 'confin[e] the claims to th[e] embodiments' found in the specification . . . ." *In re Trans Texas Holdings Corp.*, 498 F.3d 1290, 1299 (Fed. Cir. 2007) (quoting *Phillips v. AWH Corp.,* 415 F.3d 1303, 1323 (Fed. Cir. 2005), citations omitted, bracketed text in internal quotes in original); *see also Sjolund v. Musland*, 847 F.2d 1573, 1581 (Fed. Cir. 1988) ("[W]hile it is true that claims are to be interpreted *in light of* the specification and with a view to ascertaining the invention, it does not follow that limitations from the specification may be read into the claims."); *In re Bigio,* 381 F.3d 1320, 1325 (Fed Cir. 2004) ("[A]bsent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification . . . when [it] expressly disclaims the broader definition.").

Moreover, "[a]lthough an inventor is indeed free to define the specific terms used to describe his or her invention, this must be done with reasonable clarity, deliberateness, and precision." *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994) (holding that a specification generally describing desirable features and capabilities of a portable computer did not establish a specific definition for the term "computer" different from the ordinary and accustomed meaning).

However, while claims under examination must be given their broadest reasonable interpretation, in *In re Buszard*, 504 F.3d 1364, 1367 (Fed. Cir. 2007), the Federal Circuit recently reversed an anticipation rejection, holding that it was unreasonable to interpret a claim to encompass a prior art product where "a person of ordinary skill in the field" would have recognized that the two products were different, and where the specification and claims had "specifically state[d]" that the claims required a particular product. *Buszard*, 504 F.3d at 1367.

FINDINGS OF FACT

1. Claim 1 recites a method of inducing a reduced immune response to donor tissue in a transplant recipient. The transplant recipient is treated with either or both of (a) isolated fibroblasts, or (b) a supernatant from an isolated fibroblast culture, in an amount effective to reduce an immune response in the recipient to the transplanted donor tissue.

2. Claim 2 is directed to the method of claim 1, but limits the administered treating agent to isolated fibroblasts. Claim 8 recites "[t]he method of claim 2 wherein the fibroblasts are administered concurrently with administration of the transplant." Claim 9 recites "[t]he method of claim 8, wherein the fibroblasts are administered as a part of the transplant."

3. Soiffer discloses administering allogeneic bone marrow transplants to 41 leukemia patients (Soiffer 3039, abstract). Before administration, the bone marrow was treated with an antibody to remove CD6+ T cells by complement-mediated antibody lysis (*id.* at 3040, left column).

4. Bruder discloses that "bone marrow is a complex tissue comprised of hematopoietic cells, including the hematopoietic stem cells, and red and white blood cell and their precursors; and a group of cells including mesenchymal stem cells, *fibroblasts*, reticulocytes, adipocytes, and endothelial cells which contribute to the connective tissue network called 'stroma'" (Bruder, col. 4, ll. 41-47 (emphasis added)).

Thus, the bone marrow transplanted by Soiffer inherently contains fibroblasts. However, the fibroblasts in Soiffer's transplanted marrow are present in a "complex tissue" that contains a mixture of a number of different cell types.

5. The Specification does not define "isolated" or "isolated fibroblasts."

6. The Specification states:

> [I]n one aspect, the method of the present invention provides contacting the recipient of donor tissue with isolated fibroblasts. In one embodiment of this aspect, the method involves administering isolated fibroblasts to the recipient of donor tissue. The fibroblasts can be administered to the recipient before, at the same time as, or after the transplant. The fibroblasts can be either autologous or allogeneic to the recipient. The allogeneic fibroblasts can be obtained from the donor and therefore are autologous to the transplanted tissue.

(Spec. 2.)

7. The Specification also states:

> The fibroblasts can also be administered to the recipient as part of the transplant. To this objective, the present invention provides a method for reducing or ameliorating an immune response by providing to the recipient donor tissue or organ that is perfused with or includes fibroblasts. In a preferred embodiment, the fibroblasts are allogeneic to the recipient, preferably allogeneic to both donor and recipient.

(Spec. 3).

8. The Specification also states:

> [I]n the context of bone marrow (hematopoietic stem cell) transplantation, attack of the host by the graft can be reduced or eliminated. Donor marrow can be pretreated with isolated fibroblasts prior to implant of the bone marrow or peripheral blood stem cells into the recipient. The fibroblasts inhibit or reduce the T cell response such as to reduce or eliminate a recipient from being adversely affected by the donor tissue, i.e. the therapy reduces or eliminates graft versus host response.

(Spec. 7.)

ANALYSIS

We agree with the Examiner that, when given its broadest reasonable interpretation consistent with Specification, the term "isolated fibroblasts" encompasses fibroblasts which have been isolated only inasmuch as they have been separated or detached from their original source tissue, such as bone or skin.

We note that the Specification discloses a number of uses for "isolated fibroblasts," including direct administration to a recipient (*see* Finding of Fact ("FF") 6, above), as well as pretreatment of donor tissue such as bone

marrow (*see* FF 8). However, the Specification does not provide any clear or specific definition for the terms "isolated" or "isolated fibroblasts."

Thus, the present fact situation is similar to that in *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994), where the court held that a specification generally describing desirable features and capabilities of a portable computer was not sufficient to establish a specific definition for the term "computer" that differed from the ordinary and accustomed meaning. *See Paulsen*, 30 F.3d at 1480 ("Although an inventor is indeed free to define the specific terms used to describe his or her invention, this must be done with reasonable clarity, deliberateness, and precision.").

Unlike the situation in *In re Buszard*, 504 F.3d 1364, 1367 (Fed. Cir. 2007), Appellants do not point to, nor do we see, any evidence of record showing that one of ordinary skill in this art would consider "isolated fibroblasts" to exclusively mean fibroblasts that have been separated from all other cell types. Thus, nothing on the current record suggests that a person of ordinary skill would have rejected the meaning the Examiner advances (Ans. 8) as being the ordinary and accustomed meaning of the term "isolated."

Therefore, because of the absence of a specific and clear definition in the Specification, and the absence of any evidence showing that a person of ordinary skill in the art would consider the term to exclude the Soiffer's fibroblast-containing bone marrow preparation, we agree with the Examiner that "isolated fibroblasts" encompasses Soiffer's transplanted bone marrow. Thus, because Soiffer discloses treating a transplant recipient with a composition that inherently contains isolated fibroblasts, we also agree with the Examiner that Soiffer anticipates claim 1.

Appellants argue "[i]t is clear that from reading the specification, that when [Appellants] refer to isolated fibroblasts, they do not mean fibroblasts that merely are removed from the donor's bone or any other tissue where fibroblasts may be present" (Br. 4). Rather, Appellants urge, because the Specification discloses adding fibroblasts to bone marrow prior to transplantation, it is clear that they "do not intend merely to remove the fibroblasts from bone in that the fibroblasts, which can be one component of bone marrow (or from a source other than bone marrow), are used to treat another component of bone marrow, i.e., hematopoietic stem cells, in order to reduce or eliminate a graft versus host response" (*id.* at 5 (citing Spec. 7, ll. 22-27)).

Appellants contend that "the isolated fibroblasts are administered to another isolated group of cells from bone marrow, i.e., hematopoietic stem cells, in order to prevent or reduce or eliminate a graft versus host response" (Br. 6 (citing Spec. 7, ll. 22-27)), and that therefore, "when read in the context of the specification, the term 'isolated' does not read upon the mere separation of the fibroblasts from bone, as the Examiner asserts" (*id.*).

We are not persuaded by these arguments. We note that the Specification discloses an embodiment in which isolated fibroblasts are added to bone marrow before transplantation to reduce the immunogenicity of the marrow upon transplantation (*see* FF 8). However, the Specification also discloses "a method for reducing or ameliorating an immune response by providing to the recipient donor tissue or organ that is perfused with *or includes* fibroblasts. In a preferred embodiment, the fibroblasts are allogeneic to the recipient, preferably allogeneic to both donor and recipient" (Spec. 3 (emphasis added)).

Thus, in addition to the embodiment in which transplanted tissue is supplemented with previously isolated fibroblasts, the Specification also discloses a therapeutic treatment embodiment in which the transplanted tissue merely "includes" it. That is, contrary to Appellants' arguments, rather than consistently requiring the addition of fibroblasts which have been separated from other cells, the Specification clearly contemplates transplanting tissue that already contains fibroblasts autologous to the donor, as was done in Soiffer. Also, through its dependency lineage, claim 9 encompasses "isolated fibroblasts" as being "a part of the transplant."

Therefore, given the various therapeutic treatment embodiments disclosed in the Specification, we do not agree with Appellants that one of ordinary skill in the art would consider administering "isolated fibroblasts" to be limited to administering fibroblasts having any particular level of purity. Moreover, as discussed above, "while 'the specification [should be used] to interpret the meaning of a claim,' courts must not 'import[ ] limitations from the specification into the claim.' . . . [I]t is improper to 'confin[e] the claims to th[e] embodiments' found in the specification . . . ." *In re Trans Texas Holdings Corp.*, 498 F.3d 1290, 1299 (Fed. Cir. 2007) (quoting *Phillips v. AWH Corp.,* 415 F.3d 1303, 1323 (Fed.Cir.2005), citations omitted, bracketed text in internal quotes in original); *see also Sjolund v. Musland*, 847 F.2d 1573, 1581 (Fed. Cir. 1988) ("[W]hile it is true that claims are to be interpreted *in light of* the specification and with a view to ascertaining the invention, it does not follow that limitations from the specification may be read into the claims."); *In re Bigio,* 381 F.3d 1320, 1325 (Fed Cir. 2004) ("[A]bsent claim language carrying a narrow meaning,

the PTO should only limit the claim based on the specification . . . when [it] expressly disclaims the broader definition.").

In sum, we agree with the Examiner that, when given its broadest reasonable interpretation consistent with Specification, the term "isolated fibroblasts" in claim 1 encompasses fibroblasts which have been separated from their source tissue, such as skin or bone. Because the fibroblasts inherently present in Soiffer's bone marrow were isolated from the donor's bone before transplantation, they are encompassed by claim 1. Moreover, because Soiffer administers the isolated fibroblasts as part of a transplant, we agree with the Examiner that Soiffer anticipates claim 1. Because they were not argued separately from claim 1, claims 2, 4, 5, 8, 9, 11-13, 16, 17, 19, 21, 24, 26-28, 30, and 32 fall with claim 1. *See* 37 C.F.R. § 41.37(c)(1)(vii).

OBVIOUSNESS

ISSUE

Claims 6, 7, 10, 20, 22, and 31 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Soiffer and Donnelly (Ans. 4-6). The Examiner states that Soiffer "differs from the claimed invention only in that it does not teach the use of fibroblasts allogeneic to both the transplant donor and the recipient nor does it teach various different times of administration of said fibroblasts, i.e., before, during, or after BMT [(bone marrow transplantation)]" (*id.* at 5).

The Examiner cites Donnelly as teaching "that fibroblasts are immunosuppressive, interfere with lymphocyte activation, and interfere with alloimmune responses" (*id.* (citing Donnelly, abstract)). The Examiner concludes that a person of ordinary skill in the art would have considered it

obvious "to perform the BMT method of Soiffer et al, including additional fibroblasts . . . given the teachings of Donnelly et al. that fibroblasts are immunosuppressive, interfere with lymphocyte activation, and interfere with alloimmune responses" (*id.*).

The Examiner contends that, "as there are only 3 possible types/sources of fibroblasts, autologous to the recipient, autologous to the donor, or allogeneic to both, the choice of any convenient source would be obvious" (*id.*). The Examiner also contends that "the timing of administration, i.e., administration of the fibroblasts before, during, or after transplantation comprises only routine optimization that would fall well within the purview of one of skill in the art at the time of the invention" (*id.* at 5-6).

Appellants contend that Donnelly neither discloses nor remotely suggests administering "isolated fibroblasts or a supernatant from an isolated fibroblast culture in order to induce a reduced immune response against donor tissue, to reduce an immune response against recipient tissue by donor tissue, or to treat a transplant recipient for graft versus host disease," and that the combination Soiffer and Donnelly therefore fails to suggest the claimed invention (Br. 7).

The issue with respect to the obviousness rejection, therefore, is whether the Examiner erred in concluding that the combination of Soiffer and Donnelly would have rendered the subject matter of claims 6, 7, 10, 20, 22, and 31 obvious to one of ordinary skill in the art.

PRINCIPLES OF LAW

> In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. "[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references."

In re Fritch, 972 F.2d 1260, 1265 (Fed. Cir. 1992) (citations omitted, bracketed material in original).

As the Supreme Court recently pointed out, "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does . . . because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007). Thus, "[i]n determining whether obviousness is established by combining the teachings of the prior art, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art." *In re GPAC Inc.*, 57 F.3d 1573, 1581 (Fed. Cir. 1995) (internal quotations omitted).

When evaluating claims for obviousness, "the prior art as a whole must be considered. The teachings are to be viewed as they would have been viewed by one of ordinary skill." *In re Hedges*, 783 F.2d 1038, 1041 (Fed. Cir. 1986). Moreover, "'[i]t is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary

skill in the art.'" *Id.* (quoting *In re Wesslau*, 353 F.2d 238, 241 (CCPA 1965)).

FINDINGS OF FACT

9. Claims 6, 20, and 31 are directed to methods of inducing a reduced immune response to donor tissue in a transplant recipient. Claim 6 recites "[t]he method of claim 2 wherein the fibroblasts are allogeneic to both the donor of the transplant and the recipient." Claim 31 also requires a transplant recipient to be contacted with "[isolated] fibroblasts [that] are allogeneic to both the donor and recipient." Claim 20 recites a similar limitation, requiring donor tissue to be contacted with isolated fibroblasts that "are allogeneic both to the donor and to the recipient of the donor tissue."

A person of ordinary skill would therefore understand claims 6 and 31 to require treating a transplant recipient with fibroblasts which were obtained from a source other than the transplant donor and recipient. Claim 20 would be understood as requiring the transplanted tissue itself to be contacted with fibroblasts obtained from a source that is neither the donor nor the recipient of the tissue.

Because the fibroblasts administered to the bone marrow recipients in Soiffer were those that were present in the donors' marrow, the fibroblasts were therefore autologous to the marrow donors. Soiffer therefore does not meet the limitations in claims 6, 20, and 31, requiring treatment with fibroblasts that were obtained from a source other than the marrow donor and recipient.

10. Claims 7, 10, and 22 are directed to methods of inducing a reduced immune response to donor tissue in a transplant recipient, and further limit

the time at which the fibroblast cells are administered. Claim 7 recites that "the fibroblasts are administered to the recipient prior to administration of the transplant." Claim 10 recites that "the fibroblasts are administered after transplant." Claim 22 recites "the donor tissue is exposed to recipient tissue prior to being contacted with the fibroblasts."

Thus, because each of claims 7, 10, and 22 requires the transplant recipient to be contacted with fibroblasts at a different time than when the transplant recipient receives the donor tissue, the fibroblasts cannot be part of the transplanted tissue. Because Soiffer's fibroblasts were an inherent part of the transplanted marrow, Soiffer does not meet the limitations of claims 7, 10, and 22.

11. Donnelly discloses that "corneal stromal fibroblasts inhibited mixed leukocyte reactions between peripheral blood mononuclear cells of allogeneic donors, even when the corneal stromal fibroblasts were separated from the peripheral blood mononuclear cells by a 0.4 μm pore membrane" (Donnelly 157, abstract). Donnelly discloses that this inhibition was total: "[w]hen mixed leukocyte-type cultures were carried out between the panel of six mutually MLR-incompatible peripheral blood mononuclear cells and the corneal stromal fibroblast cell lines from seven different donors, no proliferative response of the peripheral blood mononuclear cells could be detected" (*id.* at 159)

12. Donnelly also discloses:

> [T]he ability of corneal stromal fibroblasts to interfere with alloimmune responses in vitro was dependent upon the continued presence of the fibroblasts and their continued production of a soluble inhibitory factor or factors. Inhibitors of allogeneic reactions that are produced by corneal stromal

> fibroblasts stimulated by immune cytokines (e.g. interferon-γ) may play a role in prolonging corneal allograft survival.

(Donnelly 157, abstract.)

13. In its evaluation of the effects of transplanting CD6-depleted bone marrow in leukemia patients, Soiffer discloses that "[n]o pre- or posttransplant immune suppressive medications for GVHD [(graft versus host disease)] prophylaxis were administered. The actuarial estimated risk of grade 2 to 4 acute GVHD was 15% in patients receiving HLA identical grafts. Chronic GVHD developed in five [of the 41 tested] patients" (Soiffer 3039, abstract). Thus, the percentage of patients receiving CD6-depleted allogeneic marrow who developed GVHD was comparable to the expected percentage in patients who receive genotypically identical marrow (*see id.* at 3041, right column, paragraph entitled "*GVHD*").

Soiffer summarizes the results of its study by stating that "[a]llogeneic transplantation with CD6 depleted bone marrow is effective in consolidating remissions of high-risk patients with acute leukemia in first remission without excessive toxicity" (Soiffer 3039, abstract).

ANALYSIS

We agree with Appellants that the Examiner has not established that the teachings of Soiffer and Donnelly would have led one of ordinary skill to practice the subject matter recited in the rejected claims.

Claims 6, 20, and 31

We note Donnelly's disclosures, that corneal stromal fibroblasts eliminate the alloimmune mixed leukocyte reaction between peripheral blood cells from unrelated donors (*see* FF 11, above), and that those fibroblasts may therefore be involved in "prolonging corneal allograft

survival" (Donnelly 157, abstract (FF 12)). However, we do not agree with the Examiner that those disclosures would have prompted a person of ordinary skill in the art practicing Soiffer's bone marrow transplantation to obtain corneal stromal fibroblasts from a third individual, who was neither the bone marrow donor nor leukemia patient/recipient, and administer those cells to the recipient.

Specifically, a person of ordinary skill viewing the prior art as a whole would have recognized that bone marrow contains fibroblasts (*see* FF 4). Thus, viewing the prior art as a whole, rather than suggesting that Soiffer's bone marrow transplants should be supplemented with corneal stromal fibroblasts, Donnelly would have suggested to one of ordinary skill in the art that Soiffer's bone already contained the immune tolerance-conferring component. The reasonableness of that conclusion would have been evidenced by Soiffer's disclosure that allogeneic bone marrow transplants were effective in treating patients without excessive toxicity even in the absence of pre- or posttransplant immune suppressive medications for GVHD (FF 13). That is, the fact that Soiffer did not need to administer immunosuppressive agents would have suggested to one of ordinary skill that the fibroblasts inherently present in Soiffer's bone marrow were acting in the immunosuppressive manner described by Donnelly.

Therefore, in our view, one of ordinary skill viewing the prior art as a whole would have reasoned from Donnelly that the fibroblasts inherently present in Soiffer's transplanted tissue permitted the effective use of allogeneic bone marrow without an excessive GVHD response in the recipient. Because one of ordinary skill in the art would have recognized from Donnelly that the fibroblasts inherently present in Soiffer's allogeneic

bone marrow already confer immune tolerance to that tissue, we do not agree with the Examiner that the cited references would have prompted one of ordinary skill performing a bone marrow transplant to obtain fibroblasts from an individual who was neither the marrow donor nor recipient, and to administer the cells to the marrow recipient.

Moreover, we are not persuaded by the Examiner's rationale that "as there are only 3 possible types/sources of fibroblasts, autologous to the recipient, autologous to the donor, or allogeneic to both, the choice of any convenient source would be obvious" (Ans. 5). Specifically, the Examiner has not provided an evidentiary basis to support his position that a person of ordinary skill in the art would have considered it obvious to supplement transplanted bone marrow with fibroblasts allogeneic to both the donor and recipient. In the case of Soiffer's allogeneic transplant, for example, we do not see, nor does the Examiner explain, why it would be convenient or desirable to undertake the effort to obtain fibroblasts from yet a third individual beyond the donor and recipient, given the fact that the donor and recipient were already at hand for the purpose of marrow donation.

Thus, viewing the cited prior art as a whole, we do not agree with the Examiner that a person of ordinary skill in the art would have considered it prima facie obvious to administer, to a transplant recipient, fibroblasts that were allogeneic to both the tissue donor and recipient. We therefore reverse the Examiner's obviousness rejection of claims 6, 20, and 31.

Claims 7, 10, 22

Each of claims 7, 10, and 22 requires the transplant recipient to be contacted with fibroblasts at a different time than when the transplant recipient receives the donor tissue (FF 10). It is the Examiner's position that

"the timing of administration, i.e., administration of the fibroblasts before, during, or after transplantation comprises only routine optimization that would fall well within the purview of one of skill in the art at the time of the invention" (Ans. 5-6).

We are not persuaded that one of ordinary skill viewing the prior art as whole would have been prompted to administer fibroblasts to a transplant recipient at a different time than when the recipient receives the donor tissue. As discussed above, in our view, a person of ordinary skill viewing the prior art as a whole would have reasoned from Donnelly that the fibroblasts inherently present in Soiffer's transplanted tissue permitted the effective use of allogeneic bone marrow without an excessive GVHD response in the recipient. Recognizing from Donnelly that the fibroblasts already present in Soiffer's allogeneic bone marrow confer immune tolerance to that tissue, a person of ordinary skill would have reasoned that there would have been no need to administer supplemental tolerance-conferring fibroblasts to the bone marrow recipient before or after the marrow transplant since such cells would have been already present.

Thus, we do not agree with the Examiner that the cited references would have prompted a person of ordinary skill to administer fibroblasts to a transplant recipient, or to transplanted tissue, before or after the recipient receives the donor tissue. We therefore reverse the Examiner's obviousness rejection of claims 7, 10, and 22.

SUMMARY

We affirm the Examiner's rejection of 1, 2, 4, 5, 8, 9, 11-13, 16, 17, 19, 21, 24, 26-28, 30, and 32 under 35 U.S.C. § 102(b) as anticipated by Soiffer, as evidenced by Bruder.

We reverse the Examiner's rejection of claims 6, 7, 10, 20, 22, and 31 under 35 U.S.C. § 103(a) as being obvious in view of Soiffer and Donnelly.

No time period for talking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

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